

Neutropaenic enterocolitis due to Methotrexate in a patient with Rheumatoid arthritis – a case report

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Abstract

Neutropaenic enterocolitis is a rare, life-threatening disease, characterised by fever and abdominal pain in the setting of neutropaenia. Neutropaenic enterocolitis as a complication of medical therapy in patients with rheumatoid arthritis has rarely been reported. Here we describe a patient with rheumatoid arthritis, who developed neutropaenic enterocolitis following a single dose of methotrexate.

Key words: Neutropaenic enterocolitis, Methotrexate, Neutropaenia, Rheumatoid arthritis

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Introduction

Neutropaenic enterocolitis (NE) is a rare, life-threatening disorder typically seen in profoundly neutropenic patients receiving cytotoxic chemotherapy(1, 2). NE is characterised by transmural inflammation, ulceration and haemorrhage leading to sepsis and bowel perforation (1, 2, 3). Here we report a case of a patient with sero-positive rheumatoid arthritis (RA), who developed NE following the commencement of Methotrexate.

Case History

A 69-year-old woman presented with a five-day

history of sore throat. By day three of admission, she had developed severe diarrhoea and right iliac fossa pain. She was recently diagnosed with sero-positive RA in addition to hypertension and chronic kidney disease (CKD). For treatment of RA she was commenced on Prednisolone 10mg daily, Methotrexate 12.5mg once weekly and folic acid 5mg daily. She had only taken a single dose of Methotrexate prior to admission.

On examination, she appeared pale, anicteric and had severe mucositis with oral candidiasis. Additionally her body mass index was low at 17kg/m². She was febrile (38.8°C) but had no palpable lymphadenopathy. Abdominal examination revealed a distended abdomen, rebound tenderness at the right lower quadrant

and absent bowel sounds. Her cardiovascular, respiratory and nervous system examinations were unremarkable. Owing to RA, she had multiple small and large joint deformities of her hands and feet without evidence of active synovitis.

Her full blood count (FBC) showed isolated leucopaenia (1810 / μ L) with a neutropaenia (390 cells/ μ L). C-reactive protein was elevated (146 mg/L). Initial resuscitation with intravenous fluids followed by intravenous meropenem, topical nystatin gel and barrier nursing care were provided.

Abdominal X-ray demonstrated multiple dilated loops of large and small bowel. In addition to pancytopenia, the patient experienced recurrent fever and abdominal distention. A non-contrast computed tomography (NCCT) abdomen revealed diffuse circumferential wall thickening of the caecum and ascending colon, causing oedematous obstruction at the ileo-caecal junction, suggestive of a diagnosis of NE (Figure 1 and Figure 2). Blood cultures, stool cultures, clostridium difficile toxin, Epstein-Barr virus, Cytomegalovirus and Human immunodeficiency virus serology tests were negative.

A nasogastric tube was placed for abdominal decompression, fluid resuscitation and total parenteral nutrition with bowel rest was provided. Intravenous antibiotics were continued and granulocyte colony-stimulating factor (GCSF) was given to treat neutropenic sepsis. She gradually recovered with normalisation of FBC by day twelve of hospital stay.

Discussion

Methotrexate, a folic acid antagonist with antiproliferative effects, is widely used to treat various malignancies and autoimmune disorders (4, 5). Pancytopenia, liver toxicity and renal impairment are well recognised adverse effects of Methotrexate (4, 5). Interestingly, Methotrexate toxicity can occur either as an idiosyncratic reaction or dose dependent reaction (4, 5). Although there are a few reported cases of NE due to RA and febrile neutropaenia following a single low dose of methotrexate, we report the first case of NE as a result of a single dose of Methotrexate having excluded other causes (1, 6-8). Several risk factors were noted to increase myelosuppression including elderly status, renal impairment, and use of non-steroidal anti-inflammatory drugs (1).

Table 1 - Blood investigations during hospital stay

	Day 1	Day 3	Day 6	Day 9	Day 12
Hb (g/dL)	11	9	7.8	8.7	10.8
MCV	84	82	79	80	86
WBC (/ μ L)	1810	1440	1150	2450	6143
Neutrophil count (/ μ L)	390	180	100	780	2400
Platelet (/ μ L)	167,000	98,000	42,000	86,000	184,000
CRP (mg/L)	146	280	353	168	68
Creatinine (μ mol/L)	160	157	168	149	146
K ⁺ (mmol/L)	5	5.2	5.6	4.8	4.5

NE has substantial mortality owing to high risk of bowel perforation and uncontrolled bleeding (8,9). The exact pathogenesis of NE remains unclear (1,2,3). NE, also known as "Typhlitis", commonly affects the caecum, ascending colon and terminal ileum (1,2).

Clinical presentation of NE can be confusing due to non-specific features such as fever, vomiting, abdominal pain and distention which may mistakenly be diagnosed as acute appendicitis (1,2). Moreover, there remains no established diagnostic criteria to identify NE (1,2,3). Hence determining the diagnosis of NE proved to be challenging (1,3) However, there is a proposed diagnostic criterion which needs further validation (Table 2) (2). Ultrasound scan and abdominal x-rays can demonstrate characteristic dilated small bowel and colon (1-5). Classic CECT findings include colonic wall thickening, nodularity and haemorrhage (1,2). NE is essentially a clinical diagnosis which is supported by CECT findings and does not require colonic biopsies (1,2). Furthermore our patient had acute on chronic kidney injury due to sepsis, which prevented her from undergoing CECT abdomen. She was also too unwell to undergo colonoscopy, which carries a high risk of perforation and bleeding (2).

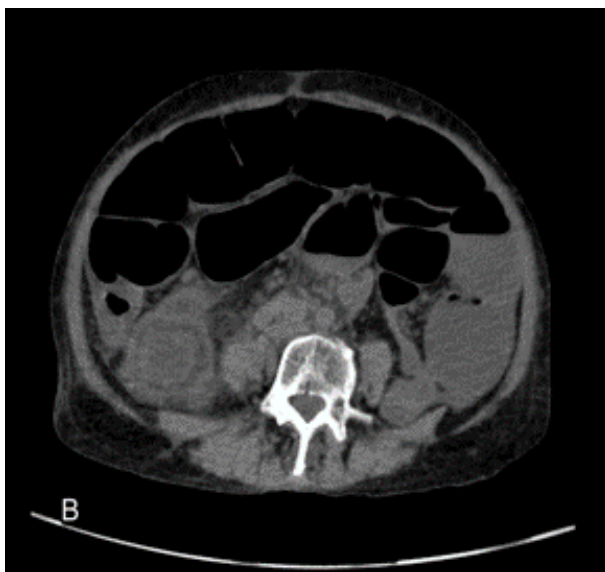


Figure 1: Cross section of NCCT abdomen showing multiple dilated ileal and jejunal bowel loops as shown by the arrows

Adequate intravenous fluid resuscitation, nasogastric suction, bowel rest with nutritional support, blood products and broad-spectrum antibiotics remain the mainstay of management of uncomplicated NE (1-4,8). Furthermore, GCSF in ill neutropenic patients augment leucocyte recovery thereby facilitating bowel healing (1,8).

Conclusions

This case study emphasises the importance of including NE as a differential diagnosis in severely immunosuppressed patients with fever and abdominal pain. Early recognition and prompt treatment of NE can vastly improve patient outcomes.

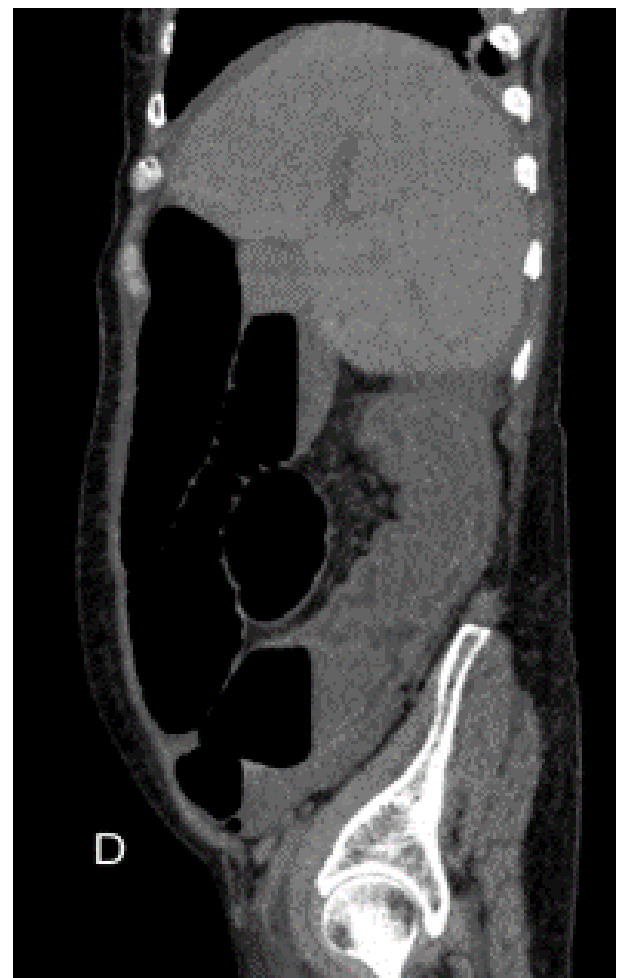


Figure 2: Sagittal view of the NCCT abdomen revealing long segment diffuse oedema of the wall of caecum and ascending colon as shown by the arrow.

Table 2 - Proposed diagnostic criteria for Necrotizing enterocolitis(2)

Major criteria
Fever (>38.3°C)
Abdominal pain
CT evidence of bowel wall thickening (>4mm thickening with up to >30mm length)
Neutropaenia (ANC <500 x 10 ⁹ cells/L)
Minor Criteria
Cramping abdominal pain
Abdominal distention
Diarrhoea
Lower gastrointestinal bleeding

Article Information

Conflicts of Interests: There are no conflicts of interest

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